

SEQUENCE LISTING

<110> TRANSGENE S.A.

<120> Novel multifunctional cytokines

<130> H2216 PCT S3

<140> PCT/EP2004/008114

<141> 2004-07-20

<150> EP 03 36 0086.7

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<150> US 60/539,320

<151> 2004-01-28

<160> 59

<170> PatentIn version 3.1

  

<210> 1

<211> 345

<212> PRT

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: fusion human IL-7/linker/human IL-2"

  

<400> 1

Met Phe His Val Ser Phe Arg Tyr Ile Phe Gly Leu Pro Pro Leu Ile  
 1 5 10 15

Leu Val Leu Leu Pro Val Ala Ser Ser Asp Cys Asp Ile Glu Gly Lys  
 20 25 30

Asp Gly Lys Gln Tyr Glu Ser Val Leu Met Val Ser Ile Asp Gln Leu  
 35 40 45

Leu Asp Ser Met Lys Glu Ile Gly Ser Asn Cys Leu Asn Asn Glu Phe  
 50 55 60

Asn Phe Phe Lys Arg His Ile Cys Asp Ala Asn Lys Glu Gly Met Phe  
 65 70 75 80

Leu Phe Arg Ala Ala Arg Lys Leu Arg Gln Phe Leu Lys Met Asn Ser  
 85 90 95  
 Thr Gly Asp Phe Asp Leu His Leu Leu Lys Val Ser Glu Gly Thr Thr  
 100 105 110  
 Ile Leu Leu Asn Cys Thr Gly Gln Val Lys Gly Arg Lys Pro Ala Ala  
 115 120 125  
 Leu Gly Glu Ala Gln Pro Thr Lys Ser Leu Glu Glu Asn Lys Ser Leu  
 130 135 140  
 Lys Glu Gln Lys Lys Leu Asn Asp Leu Cys Phe Leu Lys Arg Leu Leu  
 145 150 155 160  
 Gln Glu Ile Lys Thr Cys Trp Asn Lys Ile Leu Met Gly Thr Lys Glu  
 165 170 175  
 His Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser  
 180 185 190  
 Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu  
 195 200 205  
 Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu  
 210 215 220  
 Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile  
 225 230 235 240  
 Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe  
 245 250 255  
 Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu  
 260 265 270  
 Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys  
 275 280 285  
 Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile  
 290 295 300  
 Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala  
 305 310 315 320  
 Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe  
 325 330 335

Cys Gln Ser Ile Ile Ser Thr Leu Thr  
340 345

<210> 2

<211> 333

<212> PRT

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: fusion murine IL7/linker/murine IL-2"

<400> 2

Met Phe His Val Ser Phe Arg Tyr Ile Phe Gly Ile Pro Pro Leu Ile  
1 5 10 15

Leu Val Leu Leu Pro Val Thr Ser Ser Glu Cys His Ile Lys Asp Lys  
20 25 30

Glu Gly Lys Ala Tyr Glu Ser Val Leu Met Ile Ser Ile Asp Glu Leu  
35 40 45

Asp Lys Met Thr Gly Thr Asp Ser Asn Cys Pro Asn Asn Glu Pro Asn  
50 55 60

Phe Phe Arg Lys His Val Cys Asp Asp Thr Lys Glu Ala Ala Phe Leu  
65 70 75 80

Asn Arg Ala Ala Arg Lys Leu Lys Gln Phe Leu Lys Met Asn Ile Ser  
85 90 95

Glu Glu Phe Asn Val His Leu Leu Thr Val Ser Gln Gly Thr Gln Thr  
100 105 110

Leu Val Asn Cys Thr Ser Lys Glu Glu Lys Asn Val Lys Glu Gln Lys  
115 120 125

Lys Asn Asp Ala Cys Phe Leu Lys Arg Leu Leu Arg Glu Ile Lys Thr  
130 135 140

Cys Trp Asn Lys Ile Leu Lys Gly Ser Ile Gly Gly Gly Gly Ser Gly  
145 150 155 160

Gly Gly Gly Ser Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr Leu  
165 170 175

Thr Leu Val Leu Leu Val Asn Ser Ala Pro Thr Ser Ser Ser Thr Ser  
 180 185 190

Ser Ser Thr Ala Glu Ala Gln Gln Gln Gln Gln Gln Gln Gln  
 195 200 205

Gln Gln His Leu Glu Gln Leu Leu Met Asp Leu Gln Glu Leu Leu Ser  
 210 215 220

Arg Met Glu Asn Tyr Arg Asn Leu Lys Leu Pro Arg Met Leu Thr Phe  
 225 230 235 240

Lys Phe Tyr Leu Pro Lys Gln Ala Thr Glu Leu Lys Asp Leu Gln Cys  
 245 250 255

Leu Glu Asp Glu Leu Gly Pro Leu Arg His Val Leu Asp Leu Thr Gln  
 260 265 270

Ser Lys Ser Phe Gln Leu Glu Asp Ala Glu Asn Phe Ile Ser Asn Ile  
 275 280 285

Arg Val Thr Val Val Lys Leu Lys Gly Ser Asp Asn Thr Phe Glu Cys  
 290 295 300

Gln Phe Asp Asp Glu Ser Ala Thr Val Val Asp Phe Leu Arg Arg Trp  
 305 310 315 320

Ile Ala Phe Cys Gln Ser Ile Ile Ser Thr Ser Pro Gln  
 325 330

<210> 3

<211> 330

<212> PRT

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: fusion human  
 IL-2/linker/human IL-15"

<400> 3

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu  
 1 5 10 15

Val Thr Asn Ser Ala Pro Thr Ser Ser Thr Lys Lys Thr Gln Leu  
 20 25 30  
 Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile  
 35 40 45  
 Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe  
 50 55 60  
 Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu  
 65 70 75 80  
 Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys  
 85 90 95  
 Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile  
 100 105 110  
 Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala  
 115 120 125  
 Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe  
 130 135 140  
 Cys Gln Ser Ile Ile Ser Thr Leu Thr Gly Gly Gly Gly Ser Gly Gly  
 145 150 155 160  
 Gly Gly Ser Gly Gly Gly Gly Ser Met Arg Ile Ser Lys Pro His Leu  
 165 170 175  
 Arg Ser Ile Ser Ile Gln Cys Tyr Leu Cys Leu Leu Leu Asn Ser His  
 180 185 190  
 Phe Leu Thr Glu Ala Gly Ile His Val Phe Ile Leu Gly Cys Phe Ser  
 195 200 205  
 Ala Gly Leu Pro Lys Thr Glu Ala Asn Trp Val Asn Val Ile Ser Asp  
 210 215 220  
 Leu Lys Lys Ile Glu Asp Leu Ile Gln Ser Met His Ile Asp Ala Thr  
 225 230 235 240  
 Leu Tyr Thr Glu Ser Asp Val His Pro Ser Cys Lys Val Thr Ala Met  
 245 250 255  
 Lys Cys Phe Leu Leu Glu Leu Gln Val Ile Ser Leu Glu Ser Gly Asp  
 260 265 270

Ala Ser Ile His Asp Thr Val Glu Asn Leu Ile Ile Leu Ala Asn Asn  
 275 280 285

Ser Leu Ser Ser Asn Gly Asn Val Thr Glu Ser Gly Cys Lys Glu Cys  
 290 295 300

Glu Glu Leu Glu Glu Lys Asn Ile Lys Glu Phe Leu Gln Ser Phe Val  
 305 310 315 320

His Ile Val Gln Met Phe Ile Asn Thr Ser  
 325 330

<210> 4

<211> 330

<212> PRT

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: fusion human  
 IL-15/linker/human IL-2"

<400> 4

Met Arg Ile Ser Lys Pro His Leu Arg Ser Ile Ser Ile Gln Cys Tyr  
 1 5 10 15

Leu Cys Leu Leu Leu Asn Ser His Phe Leu Thr Glu Ala Gly Ile His  
 20 25 30

Val Phe Ile Leu Gly Cys Phe Ser Ala Gly Leu Pro Lys Thr Glu Ala  
 35 40 45

Asn Trp Val Asn Val Ile Ser Asp Leu Lys Lys Ile Glu Asp Leu Ile  
 50 55 60

Gln Ser Met His Ile Asp Ala Thr Leu Tyr Thr Glu Ser Asp Val His  
 65 70 75 80

Pro Ser Cys Lys Val Thr Ala Met Lys Cys Phe Leu Leu Glu Leu Gln  
 85 90 95

Val Ile Ser Leu Glu Ser Gly Asp Ala Ser Ile His Asp Thr Val Glu  
 100 105 110

Asn Leu Ile Ile Leu Ala Asn Asn Ser Leu Ser Ser Asn Gly Asn Val  
 115 120 125

Thr Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu Glu Glu Lys Asn Ile  
 130 135 140

Lys Glu Phe Leu Gln Ser Phe Val His Ile Val Gln Met Phe Ile Asn  
 145 150 155 160

Thr Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly  
 165 170 175

Ser Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala  
 180 185 190

Leu Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln  
 195 200 205

Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly  
 210 215 220

Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys  
 225 230 235 240

Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu  
 245 250 255

Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser  
 260 265 270

Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val  
 275 280 285

Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr  
 290 295 300

Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr  
 305 310 315 320

Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr  
 325 330

<210> 5

<211> 350

<212> PRT

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: fusion signal IL-2/  
human IL-15/linker/human IL-2"

<400> 5

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala,Leu Ser Leu Ala Leu  
1 5 10 15

Val Thr Asn Ser Met Arg Ile Ser Lys Pro His Leu Arg Ser Ile Ser  
20 25 30

Ile Gln Cys Tyr Leu Cys Leu Leu Leu Asn Ser His Phe Leu Thr Glu  
35 40 45

Ala Gly Ile His Val Phe Ile Leu Gly Cys Phe Ser Ala Gly Leu Pro  
50 55 60

Lys Thr Glu Ala Asn Trp Val Asn Val Ile Ser Asp Leu Lys Lys Ile  
65 70 75 80

Glu Asp Leu Ile Gln Ser Met His Ile Asp Ala,Thr Leu Tyr Thr Glu  
85 90 95

Ser Asp Val His Pro Ser Cys Lys Val Thr Ala Met Lys Cys Phe Leu  
100 105 110

Leu Glu Leu Gln Val Ile Ser Leu Glu Ser Gly Asp Ala Ser Ile His  
115 120 125

Asp Thr Val Glu Asn Leu Ile Ile Leu Ala Asn Asn Ser Leu Ser Ser  
130 135 140

Asn Gly Asn Val Thr Glu Ser Gly Cys Lys Glu Cys Glu Glu Leu Glu  
145 150 155 160

Glu Lys Asn Ile Lys Glu Phe Leu Gln Ser Phe,Val His Ile Val Gln  
165 170 175

Met Phe Ile Asn Thr Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser  
180 185 190

Gly Gly Gly Gly Ser Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala  
195 200 205



Leu Ser Leu Ala Leu Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr  
210 215 220

Lys Lys Thr Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met  
225 230 235 240

Ile Leu Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met  
245 250 255

Leu Thr Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His  
260 265 270

Leu Gln Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn  
275 280 285

Leu Ala Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser  
290 295 300

Asn Ile Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe  
305 310 315 320

Met Cys Glu Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn  
325 330 335

Arg Trp Ile Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr  
340 345 350

<210> 6

$\langle 211 \rangle$     324

<212> PRT

<213> artificial sequence

<220>

&lt;221&gt; source

<223> /note= "Description of artificial sequence: fusion murine IL-2/linker/murine IL-15"

<400> 6

Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr Leu Thr Leu Val Leu  
1 5 10 15

Leu Val Asn Ser Ala Pro Thr Ser Ser Ser Thr Ser Ser Ser Thr Ala  
20 25 30

Glu Ala Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln His Leu  
35 40 45

Glu Gln Leu Leu Met Asp Leu Gln Glu Leu Leu Ser Arg Met Glu Asn  
50 55 60

Tyr Arg Asn Leu Lys Leu Pro Arg Met Leu Thr Phe Lys Phe Tyr Leu  
65 70 75 80

Pro Lys Gln Ala Thr Glu Leu Lys Asp Leu Gln Cys Leu Glu Asp Glu  
85 90 95

Leu Gly Pro Leu Arg His Val Leu Asp Leu Thr Gln Ser Lys Ser Phe  
100 105 110

Gln Leu Glu Asp Ala Glu Asn Phe Ile Ser Asn Ile Arg Val Thr Val  
115 120 125

Val Lys Leu Lys Gly Ser Asp Asn Thr Phe Glu Cys Gln Phe Asp Asp  
130 135 140

Glu Ser Ala Thr Val Val Asp Phe Leu Arg Arg Trp Ile Ala Phe Cys  
145 150 155 160

Gln Ser Ile Ile Ser Thr Ser Pro Gln Gly Gly Gly Gly Ser Gly Gly  
165 170 175

Gly Gly Ser Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr Leu Thr  
180 185 190

Leu Val Leu Leu Val Asn Ser Ala Gly Ala Asn Trp Ile Asp Val Arg  
195 200 205

Tyr Asp Leu Glu Lys Ile Glu Ser Leu Ile Gln Ser Ile His Ile Asp  
210 215 220

Thr Thr Leu Tyr Thr Asp Ser Asp Phe His Pro Ser Cys Lys Val Thr  
225 230 235 240

Ala Met Asn Cys Phe Leu Leu Glu Leu Gln Val Ile Leu His Glu Tyr  
245 250 255

Ser Asn Met Thr Leu Asn Glu Thr Val Arg Asn Val Leu Tyr Leu Ala  
260 265 270

Asn Ser Thr Leu Ser Ser Asn Lys Asn Val Ala Glu Ser Gly Cys Lys  
275 280 285

Glu Cys Glu Glu Leu Glu Glu Lys Thr Phe Thr Glu Phe Leu Gln Ser  
 290 295 300

Phe Ile Arg Ile Val Gln Met Phe Ile Asn Thr Ser Asp Tyr Lys Asp  
 305 310 315 320

Asp Asp Asp Lys

<210> 7

<211> 324

<212> PRT

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: fusion murine  
 IL-15/linker/murine IL-2"

<400> 7

Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr Leu Thr Leu Val Leu  
 1 5 10 15

Leu Val Asn Ser Ala Gly Ala Asn Trp Ile Asp Val Arg Tyr Asp Leu  
 20 25 30

Glu Lys Ile Glu Ser Leu Ile Gln Ser Ile His Ile Asp Thr Thr Leu  
 35 40 45

Tyr Thr Asp Ser Asp Phe His Pro Ser Cys Lys Val Thr Ala Met Asn  
 50 55 60

Cys Phe Leu Leu Glu Leu Gln Val Ile Leu His Glu Tyr Ser Asn Met  
 65 70 75 80

Thr Leu Asn Glu Thr Val Arg Asn Val Leu Tyr Leu Ala Asn Ser Thr  
 85 90 95

Leu Ser Ser Asn Lys Asn Val Ala Glu Ser Gly Cys Lys Glu Cys Glu  
 100 105 110

Glu Leu Glu Glu Lys Thr Phe Thr Glu Phe Leu Gln Ser Phe Ile Arg  
 115 120 125

Ile Val Gln Met Phe Ile Asn Thr Ser Asp Tyr Lys Asp Asp Asp Asp  
 130 135 140

Lys Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Met Tyr Ser Met Gln  
 145 150 155' 160

Leu Ala Ser Cys Val Thr Leu Thr Leu Val Leu Leu Val Asn Ser Ala  
 165 170 175

Pro Thr Ser Ser Ser Thr Ser Ser Ser Thr Ala Glu Ala Gln Gln Gln  
 180 185 190

Gln Gln Gln Gln Gln Gln Gln Gln Gln His Leu Glu Gln Leu Leu Met  
 195 200 205

Asp Leu Gln Glu Leu Leu Ser Arg Met Glu Asn Tyr Arg Asn Leu Lys  
 210 215 220

Leu Pro Arg Met Leu Thr Phe Lys Phe Tyr Leu Pro Lys Gln Ala Thr  
 225 230 235' 240

Glu Leu Lys Asp Leu Gln Cys Leu Glu Asp Glu Leu Gly Pro Leu Arg  
 245 250 255

His Val Leu Asp Leu Thr Gln Ser Lys Ser Phe Gln Leu Glu Asp Ala  
 260 265 270

Glu Asn Phe Ile Ser Asn Ile Arg Val Thr Val Val Lys Leu Lys Gly  
 275 280 285

Ser Asp Asn Thr Phe Glu Cys Gln Phe Asp Asp Glu Ser Ala Thr Val  
 290 295 300

Val Asp Phe Leu Arg Arg Trp Ile Ala Phe Cys Gln Ser Ile Ile Ser  
 305 310 315' 320

Thr Ser Pro Gln

<210> 8

<211> 361

<212> PRT

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: fusion human  
 IL-2/linker/human pro IL-18"

&lt;400&gt; 8

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu  
 1 5 10 15

Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu  
 20 25 30

Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile  
 35 40 45

Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe  
 50 55 60

Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu  
 65 70 75 80

Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys  
 85 90 95

Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile  
 100 105 110

Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala  
 115 120 125

Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe  
 130 135 140

Cys Gln Ser Ile Ile Ser Thr Leu Thr Gly Gly Gly Gly Ser Gly Gly  
 145 150 155 160

Gly Gly Ser Gly Gly Gly Gly Ser Met Ala Ala Glu Pro Val Glu Asp  
 165 170 175

Asn Cys Ile Asn Phe Val Ala Met Lys Phe Ile Asp Asn Thr Leu Tyr  
 180 185 190

Phe Ile Ala Glu Asp Asp Glu Asn Leu Glu Ser Asp Tyr Phe Gly Lys  
 195 200 205

Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn Asp Gln Val Leu  
 210 215 220

Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp Met Thr Asp Ser  
 225 230 235 240

Asp Cys Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile Ile Ser Met Tyr  
                   245                  250                  255

Lys Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile Ser Val Lys Cys  
                   260                  265                  270

Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile Ile Ser Phe Lys  
                   275                  280                  285

Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys Ser Asp Ile Ile  
                   290                  295                  300

Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys Met Gln Phe Glu  
   305                  310                  315                  320

Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu Lys Glu Arg Asp  
                   325                  330                  335

Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu Gly Asp Arg Ser  
                   340                  345                  350

Ile Met Phe Thr Val Gln Asn Glu Asp  
                   355                  360

<210> 9

<211> 361

<212> PRT

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: fusion human  
 IL-2/linker/ human pro IL-18 K89A"

<400> 9

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu  
   1                  5                  10                  15

Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu  
                   20                  25                  30

Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met, Ile Leu Asn Gly Ile  
                   35                  40                  45

Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe  
 50 55 60

Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu  
 65 70 75 80

Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys  
 85 90 95

Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile  
 100 105 110

Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala  
 115 120 125

Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe  
 130 135 140

Cys Gln Ser Ile Ile Ser Thr Leu Thr Gly Gly Gly Gly Ser Gly Gly  
 145 150 155 160

Gly Gly Ser Gly Gly Gly Gly Ser Met Ala Ala Glu Pro Val Glu Asp  
 165 170 175

Asn Cys Ile Asn Phe Val Ala Met Lys Phe Ile Asp Asn Thr Leu Tyr  
 180 185 190

Phe Ile Ala Glu Asp Asp Glu Asn Leu Glu Ser Asp Tyr Phe Gly Lys  
 195 200 205

Leu Glu Ser Lys Leu Ser Val Ile Arg Asn Leu Asn Asp Gln Val Leu  
 210 215 220

Phe Ile Asp Gln Gly Asn Arg Pro Leu Phe Glu Asp Met Thr Asp Ser  
 225 230 235 240

Asp Cys Arg Asp Asn Ala Pro Arg Thr Ile Phe Ile Ile Ser Met Tyr  
 245 250 255

Ala Asp Ser Gln Pro Arg Gly Met Ala Val Thr Ile Ser Val Lys Cys  
 260 265 270

Glu Lys Ile Ser Thr Leu Ser Cys Glu Asn Lys Ile Ile Ser Phe Lys  
 275 280 285

Glu Met Asn Pro Pro Asp Asn Ile Lys Asp Thr Lys Ser Asp Ile Ile  
 290 295 300

Phe Phe Gln Arg Ser Val Pro Gly His Asp Asn Lys Met Gln Phe Glu  
305 310 315 320

Ser Ser Ser Tyr Glu Gly Tyr Phe Leu Ala Cys Glu Lys Glu Arg Asp  
325 330 335

Leu Phe Lys Leu Ile Leu Lys Lys Glu Asp Glu Leu Gly Asp Arg Ser  
340 345 350

Ile Met Phe Thr Val Gln Asn Glu Asp  
355 360

<210> 10

<211> 325

<212> PRT

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: fusion human  
IL-2/linker/mature human IL-18"

<400> 10

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala'Leu Ser Leu Ala Leu  
1 5 10 15

Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu  
20 25 30

Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile  
35 40 45

Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe  
50 55 60

Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu  
65 70 75 80

Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn'Leu Ala Gln Ser Lys  
85 90 95

Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile  
100 105 110



Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala  
 115 120 125

Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe  
 130 135 140

Cys Gln Ser Ile Ile Ser Thr Leu Thr Gly Gly Gly Gly Ser Gly Gly  
 145 150 155 160

Gly Gly Ser Gly Gly Gly Gly Ser Tyr Phe Gly Lys Leu Glu Ser Lys  
 165 170 175

Leu Ser Val Ile Arg Asn Leu Asn Asp Gln Val Leu Phe Ile Asp Gln  
 180 185 190

Gly Asn Arg Pro Leu Phe Glu Asp Met Thr Asp Ser Asp Cys Arg Asp  
 195 200 205

Asn Ala Pro Arg Thr Ile Phe Ile Ile Ser Met Tyr Lys Asp Ser Gln  
 210 215 220

Pro Arg Gly Met Ala Val Thr Ile Ser Val Lys Cys Glu Lys Ile Ser  
 225 230 235 240

Thr Leu Ser Cys Glu Asn Lys Ile Ile Ser Phe Lys Glu Met Asn Pro  
 245 250 255

Pro Asp Asn Ile Lys Asp Thr Lys Ser Asp Ile Ile Phe Phe Gln Arg  
 260 265 270

Ser Val Pro Gly His Asp Asn Lys Met Gln Phe Glu Ser Ser Ser Tyr  
 275 280 285

Glu Gly Tyr Phe Leu Ala Cys Glu Lys Glu Arg Asp Leu Phe Lys Leu  
 290 295 300

Ile Leu Lys Lys Glu Asp Glu Leu Gly Asp Arg Ser Ile Met Phe Thr  
 305 310 315 320

Val Gln Asn Glu Asp  
 325

<210> 11

<211> 325

<212> PRT

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: fusion human IL-2/linker/ mature human IL-18 K89A"

<400> 11

Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu Ala Leu  
1 5 10 15

Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr Gln Leu  
20 25 30

Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn Gly Ile  
35 40 45

Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe Lys Phe  
50 55 60

Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys Leu Glu  
65 70 75 80

Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln Ser Lys  
85 90 95

Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn Val Ile  
100 105 110

Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu Tyr Ala  
115 120 125

Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile Thr Phe  
130 135 140

Cys Gln Ser Ile Ile Ser Thr Leu Thr Gly Gly Gly Gly Ser Gly Gly  
145 150 155 160

Gly Gly Ser Gly Gly Gly Gly Ser Tyr Phe Gly Lys Leu Glu Ser Lys  
165 170 175

Leu Ser Val Ile Arg Asn Leu Asn Asp Gln Val Leu Phe Ile Asp Gln  
180 185 190

Gly Asn Arg Pro Leu Phe Glu Asp Met Thr Asp Ser Asp Cys Arg Asp  
195 200 205

Asn Ala Pro Arg Thr Ile Phe Ile Ile Ser Met Tyr Ala Asp Ser Gln  
 210 215 220

Pro Arg Gly Met Ala Val Thr Ile Ser Val Lys Cys Glu Lys Ile Ser  
 225 230 235 240

Thr Leu Ser Cys Glu Asn Lys Ile Ile Ser Phe Lys Glu Met Asn Pro  
 245 250 255

Pro Asp Asn Ile Lys Asp Thr Lys Ser Asp Ile Ile Phe Phe Gln Arg  
 260 265 270

Ser Val Pro Gly His Asp Asn Lys Met Gln Phe Glu Ser Ser Ser Tyr  
 275 280 285

Glu Gly Tyr Phe Leu Ala Cys Glu Lys Glu Arg Asp Leu Phe Lys Leu  
 290 295 300

Ile Leu Lys Lys Glu Asp Glu Leu Gly Asp Arg Ser Ile Met Phe Thr  
 305 310 315 320

Val Gln Asn Glu Asp  
 325

<210> 12

<211> 371

<212> PRT

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: fusion murine  
 IL-2/linker/murine pro-IL-18"

<400> 12

Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr Leu Thr Leu Val Leu  
 1 5 10 15

Leu Val Asn Ser Ala Pro Thr Ser Ser Ser Thr Ser Ser Thr Ala  
 20 25 30

Glu Ala Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln His Leu  
 35 40 45

Glu Gln Leu Leu Met Asp Leu Gln Glu Leu Leu Ser Arg Met Glu Asn  
 50 55 60

Tyr Arg Asn Leu Lys Leu Pro Arg Met Leu Thr Phe Lys Phe Tyr Leu  
65 70 75 80

Pro Lys Gln Ala Thr Glu Leu Lys Asp Leu Gln Cys Leu Glu Asp Glu  
85 90 95

Leu Gly Pro Leu Arg His Val Leu Asp Leu Thr Gln Ser Lys Ser Phe  
100 105 110

Gln Leu Glu Asp Ala Glu Asn Phe Ile Ser Asn Ile Arg Val Thr Val  
115 120 125

Val Lys Leu Lys Gly Ser Asp Asn Thr Phe Glu Cys Gln Phe Asp Asp  
130 135 140

Glu Ser Ala Thr Val Val Asp Phe Leu Arg Arg Trp Ile Ala Phe Cys  
145 150 155 160

Gln Ser Ile Ile Ser Thr Ser Pro Gln Gly Gly Gly Gly Ser Gly Gly  
165 170 175

Gly Gly Ser Met Ala Ala Met Ser Glu Asp Ser Cys Val Asn Phe Lys  
180 185 190

Glu Met Met Phe Ile Asp Asn Thr Leu Tyr Phe Ile Pro Glu Glu Asn  
195 200 205

Gly Asp Leu Glu Ser Asp Asn Phe Gly Arg Leu His Cys Thr Thr Ala  
210 215 220

Val Ile Arg Asn Ile Asn Asp Gln Val Leu Phe Val Asp Lys Arg Gln  
225 230 235 240

Pro Val Phe Glu Asp Met Thr Asp Ile Asp Gln Ser Ala Ser Glu Pro  
245 250 255

Gln Thr Arg Leu Ile Ile Tyr Met Tyr Lys Asp Ser Glu Val Arg Gly  
260 265 270

Leu Ala Val Thr Leu Ser Val Lys Asp Ser Lys Met Ser Thr Leu Ser  
275 280 285

Cys Lys Asn Lys Ile Ile Ser Phe Glu Glu Met Asp Pro Pro Glu Asn  
290 295 300

Ile Asp Asp Ile Gln Ser Asp Leu Ile Phe Phe Gln Lys Arg Val Pro  
 305 310 315 320

Gly His Asn Lys Met Glu Phe Glu Ser Ser Leu Tyr Glu Gly His Phe  
 325 330 335

Leu Ala Cys Gln Lys Glu Asp Asp Ala Phe Lys Leu Ile Leu Lys Lys  
 340 345 350

Lys Asp Glu Asn Gly Asp Lys Ser Val Met Phe Thr Leu Thr Asn Leu  
 355 360 365

His Gln Ser  
 370

<210> 13

<211> 371

<212> PRT

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: fusion murine  
 IL-2/linker/murine pro IL-18 K89A"

<400> 13

Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr Leu Thr Leu Val Leu

1 5 10 15

Leu Val Asn Ser Ala Pro Thr Ser Ser Ser Thr Ser Ser Ser Thr Ala  
 20 25 30

Glu Ala Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln His Leu  
 35 40 45

Glu Gln Leu Leu Met Asp Leu Gln Glu Leu Leu Ser Arg Met Glu Asn  
 50 55 60

Tyr Arg Asn Leu Lys Leu Pro Arg Met Leu Thr Phe Lys Phe Tyr Leu  
 65 70 75 80

Pro Lys Gln Ala Thr Glu Leu Lys Asp Leu Gln Cys Leu Glu Asp Glu  
 85 90 95

Leu Gly Pro Leu Arg His Val Leu Asp Leu Thr Gln Ser Lys Ser Phe  
 100 105 110

Gln Leu Glu Asp Ala Glu Asn Phe Ile Ser Asn Ile Arg Val Thr Val  
 115 120 125

Val Lys Leu Lys Gly Ser Asp Asn Thr Phe Glu Cys Gln Phe Asp Asp  
 130 135 140

Glu Ser Ala Thr Val Val Asp Phe Leu Arg Arg Trp Ile Ala Phe Cys  
 145 150 155 160

Gln Ser Ile Ile Ser Thr Ser Pro Gln Gly Gly Gly Gly Ser Gly Gly  
 165 170 175

Gly Gly Ser Met Ala Ala Met Ser Glu Asp Ser Cys Val Asn Phe Lys  
 180 185 190

Glu Met Met Phe Ile Asp Asn Thr Leu Tyr Phe Ile Pro Glu Glu Asn  
 195 200 205

Gly Asp Leu Glu Ser Asp Asn Phe Gly Arg Leu His Cys Thr Thr Ala  
 210 215 220

Val Ile Arg Asn Ile Asn Asp Gln Val Leu Phe Val Asp Lys Arg Gln  
 225 230 235 240

Pro Val Phe Glu Asp Met Thr Asp Ile Asp Gln Ser Ala Ser Glu Pro  
 245 250 255

Gln Thr Arg Leu Ile Ile Tyr Met Tyr Ala Asp Ser Glu Val Arg Gly  
 260 265 270

Leu Ala Val Thr Leu Ser Val Lys Asp Ser Lys Met Ser Thr Leu Ser  
 275 280 285

Cys Lys Asn Lys Ile Ile Ser Phe Glu Glu Met Asp Pro Pro Glu Asn  
 290 295 300

Ile Asp Asp Ile Gln Ser Asp Leu Ile Phe Phe Gln Lys Arg Val Pro  
 305 310 315 320

Gly His Asn Lys Met Glu Phe Glu Ser Ser Leu Tyr Glu Gly His Phe  
 325 330 335

Leu Ala Cys Gln Lys Glu Asp Asp Ala Phe Lys Leu Ile Leu Lys Lys  
 340 345 350

Lys Asp Glu Asn Gly Asp Lys Ser Val Met Phe Thr Leu Thr Asn Leu  
 355 360 365

His Gln Ser  
 370

<210> 14

<211> 336

<212> PRT

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: fusion murine  
 IL-2/linker/ mature murine IL-18"

<400> 14

Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr Leu Thr Leu Val Leu  
 1 5 10 15

Leu Val Asn Ser Ala Pro Thr Ser Ser Ser Thr Ser Ser Ser Thr Ala  
 20 25 30

Glu Ala Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln His Leu  
 35 40 45

Glu Gln Leu Leu Met Asp Leu Gln Glu Leu Leu Ser Arg Met Glu Asn  
 50 55 60

Tyr Arg Asn Leu Lys Leu Pro Arg Met Leu Thr Phe Lys Phe Tyr Leu  
 65 70 75 80

Pro Lys Gln Ala Thr Glu Leu Lys Asp Leu Gln Cys Leu Glu Asp Glu  
 85 90 95

Leu Gly Pro Leu Arg His Val Leu Asp Leu Thr Gln Ser Lys Ser Phe  
 100 105 110

Gln Leu Glu Asp Ala Glu Asn Phe Ile Ser Asn Ile Arg Val Thr Val  
 115 120 125

Val Lys Leu Lys Gly Ser Asp Asn Thr Phe Glu Cys Gln Phe Asp Asp  
 130 135 140

Glu Ser Ala Thr Val Val Asp Phe Leu Arg Arg Trp Ile Ala Phe Cys  
 145 150 155 160

Gln Ser Ile Ile Ser Thr Ser Pro Gln Gly Gly Gly Gly Ser Gly Gly  
 165 170 175

Gly Gly Ser Asn Phe Gly Arg Leu His Cys Thr Thr Ala Val Ile Arg  
 180 185 190

Asn Ile Asn Asp Gln Val Leu Phe Val Asp Lys Arg Gln Pro Val Phe  
 195 200 205

Glu Asp Met Thr Asp Ile Asp Gln Ser Ala Ser Glu Pro Gln Thr Arg  
 210 215 220

Leu Ile Ile Tyr Met Tyr Lys Asp Ser Glu Val Arg Gly Leu Ala Val  
 225 230 235 240

Thr Leu Ser Val Lys Asp Ser Lys Met Ser Thr Leu Ser Cys Lys Asn  
 245 250 255

Lys Ile Ile Ser Phe Glu Glu Met Asp Pro Pro Glu Asn Ile Asp Asp  
 260 265 270

Ile Gln Ser Asp Leu Ile Phe Phe Gln Lys Arg Val Pro Gly His Asn  
 275 280 285

Lys Met Glu Phe Glu Ser Ser Leu Tyr Glu Gly His Phe Leu Ala Cys  
 290 295 300

Gln Lys Glu Asp Asp Ala Phe Lys Leu Ile Leu Lys Lys Lys Asp Glu  
 305 310 315 320

Asn Gly Asp Lys Ser Val Met Phe Thr Leu Thr Asn Leu His Gln Ser  
 325 330 335

<210> 15

<211> 336

<212> PRT

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: fusion murine  
 IL-2/linker/mature murine IL-18 K89A"



&lt;400&gt; 15

Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr Leu Thr Leu Val Leu  
1 5 10 15

Leu Val Asn Ser Ala Pro Thr Ser Ser Ser Thr Ser Ser Ser Thr Ala  
20 25 30

Glu Ala Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln His Leu  
35 40 45

Glu Gln Leu Leu Met Asp Leu Gln Glu Leu Leu Ser Arg Met Glu Asn  
50 55 60

Tyr Arg Asn Leu Lys Leu Pro Arg Met Leu Thr Phe Lys Phe Tyr Leu  
65 70 75 80

Pro Lys Gln Ala Thr Glu Leu Lys Asp Leu Gln Cys Leu Glu Asp Glu  
85 90 95

Leu Gly Pro Leu Arg His Val Leu Asp Leu Thr Gln Ser Lys Ser Phe  
100 105 110

Gln Leu Glu Asp Ala Glu Asn Phe Ile Ser Asn Ile Arg Val Thr Val  
115 120 125

Val Lys Leu Lys Gly Ser Asp Asn Thr Phe Glu Cys Gln Phe Asp Asp  
130 135 140

Glu Ser Ala Thr Val Val Asp Phe Leu Arg Arg Trp Ile Ala Phe Cys  
145 150 155 160

Gln Ser Ile Ile Ser Thr Ser Pro Gln Gly Gly Gly Gly Ser Gly Gly  
165 170 175

Gly Gly Ser Asn Phe Gly Arg Leu His Cys Thr Thr Ala Val Ile Arg  
180 185 190

Asn Ile Asn Asp Gln Val Leu Phe Val Asp Lys Arg Gln Pro Val Phe  
195 200 205

Glu Asp Met Thr Asp Ile Asp Gln Ser Ala Ser Glu Pro Gln Thr Arg  
210 215 220

Leu Ile Ile Tyr Met Tyr Ala Asp Ser Glu Val Arg Gly Leu Ala Val  
225 230 235 240

Thr Leu Ser Val Lys Asp Ser Lys Met Ser Thr Leu Ser Cys Lys Asn  
                   245                  250                  255

Lys Ile Ile Ser Phe Glu Glu Met Asp Pro Pro Glu Asn Ile Asp Asp  
                   260                  265                  270

Ile Gln Ser Asp Leu Ile Phe Phe Gln Lys Arg Val Pro Gly His Asn  
                   275                  280                  285

Lys Met Glu Phe Glu Ser Ser Leu Tyr Glu Gly His Phe Leu Ala Cys  
           290                  295                  300

Gln Lys Glu Asp Asp Ala Phe Lys Leu Ile Leu Lys Lys Lys Asp Glu  
   305                  310                  315                  320

Asn Gly Asp Lys Ser Val Met Phe Thr Leu Thr Asn Leu His Gln Ser  
                   325                  330                  335

<210> 16

<211> 347

<212> PRT

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: fusion human  
 IL-21/linker/ human IL-2"

<400> 16

Met Ala Ala Leu Gln Lys Ser Val Ser Ser Phe Leu Met Gly Thr Leu  
   1                  5                  10                  15

Ala Thr Ser Cys Leu Leu Leu Leu Ala Leu Leu Val Gln Gly Gly Ala  
           20                  25                  30

Ala Ala Pro Ile Ser Ser His Cys Arg Leu Asp Lys Ser Asn Phe Gln  
           35                  40                  45

Gln Pro Tyr Ile Thr Asn Arg Thr Phe Met Leu Ala Lys Glu Ala Ser  
   50                  55                  60

Leu Ala Asp Asn Asn Thr Asp Val Arg Leu Ile Gly Glu Lys Leu Phe  
   65                  70                  75                  80

His Gly Val Ser Met Ser Glu Arg Cys Tyr Leu Met Lys Gln Val Leu  
           85                  90                  95

Asn Phe Thr Leu Glu Glu Val Leu Phe Pro Gln Ser Asp Arg Phe Gln  
 100 105 110

Pro Tyr Met Gln Glu Val Val Pro Phe Leu Ala Arg Leu Ser Asn Arg  
 115 120 125

Leu Ser Thr Cys His Ile Glu Gly Asp Asp Leu His Ile Gln Arg Asn  
 130 135 140

Val Gln Lys Leu Lys Asp Thr Val Lys Lys Leu Gly Glu Ser Gly Glu  
 145 150 155 160

Ile Lys Ala Ile Gly Glu Leu Asp Leu Leu Phe Met Ser Leu Arg Asn  
 165 170 175

Ala Cys Ile Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Gly Gly Gly  
 180 185 190

Gly Ser Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala Leu Ser Leu  
 195 200 205

Ala Leu Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr Lys Lys Thr  
 210 215 220

Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met Ile Leu Asn  
 225 230 235 240

Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met Leu Thr Phe  
 245 250 255

Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His Leu Gln Cys  
 260 265 270

Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn Leu Ala Gln  
 275 280 285

Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser Asn Ile Asn  
 290 295 300

Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe Met Cys Glu  
 305 310 315 320

Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn Arg Trp Ile  
 325 330 335

Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr  
 340 345

<210> 17

<211> 325

<212> PRT

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: fusion murine  
 IL-21/linker/murine IL-2"

<400> 17

Met Glu Arg Thr Leu Val Cys Leu Val Val Ile Phe Leu Gly Thr Val  
 1 5 10 15

Ala His Lys Ser Ser Pro Gln Gly Pro Asp Arg Leu Leu Ile Arg Leu  
 20 25 30

Arg His Leu Ile Asp Ile Val Glu Gln Leu Lys Ile Tyr Glu Asn Asp  
 35 40 45

Leu Asp Pro Glu Leu Leu Ser Ala Pro Gln Asp Val Lys Gly His Cys  
 50 55 60

Glu His Ala Ala Phe Ala Cys Phe Gln Lys Ala Lys Leu Lys Pro Ser  
 65 70 75 80

Asn Pro Gly Asn Asn Lys Thr Phe Ile Ile Asp Leu Val Ala Gln Leu  
 85 90 95

Arg Arg Arg Leu Pro Ala Arg Arg Gly Gly Lys Lys Gln Lys His Ile  
 100 105 110

Ala Lys Cys Pro Ser Cys Asp Ser Tyr Glu Lys Arg Thr Pro Lys Glu  
 115 120 125

Phe Leu Glu Arg Leu Lys Trp Leu Leu Gln Lys Met Ile His Gln His  
 130 135 140

Leu Ser Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser Met Tyr Ser Met  
 145 150 155 160

Gln Leu Ala Ser Cys Val Thr Leu Thr Leu Val Leu Leu Val Asn Ser  
                   165                                  170                  175

Ala Pro Thr Ser Ser Ser Thr Ser Ser Ser Thr Ala Glu Ala Gln Gln  
                   180                                  185                  190

Gln Gln Gln Gln Gln Gln Gln Gln Gln Gln His Leu Glu Gln Leu Leu  
                   195                                  200                  205

Met Asp Leu Gln Glu Leu Leu Ser Arg Met Glu Asn Tyr Arg Asn Leu  
           210                                  215                  220

Lys Leu Pro Arg Met Leu Thr Phe Lys Phe Tyr Leu Pro Lys Gln Ala  
   225                                  230                  235                  240

Thr Glu Leu Lys Asp Leu Gln Cys Leu Glu Asp Glu Leu Gly Pro Leu  
                   245                                  250                  255

Arg His Val Leu Asp Leu Thr Gln Ser Lys Ser Phe Gln Leu Glu Asp  
                   260                                  265                  270

Ala Glu Asn Phe Ile Ser Asn Ile Arg Val Thr Val Val Lys Leu Lys  
                   275                                  280                  285

Gly Ser Asp Asn Thr Phe Glu Cys Gln Phe Asp Asp Glu Ser Ala Thr  
           290                                  295                  300

Val Val Asp Phe Leu Arg Arg Trp Ile Ala Phe Cys Gln Ser Ile Ile  
   305                                  310                  315                  320

Ser Thr Ser Pro Gln  
                   325

<210> 18

<211> 334

<212> PRT

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: fusion human  
           IFN-g/linker/human IL-2"

<400> 18

Met Lys Tyr Thr Ser Tyr Ile Leu Ala Phe Gln Leu Cys Ile Val Leu  
   1                  5                  10                  15

Gly Ser Leu Gly Cys Tyr Cys Gln Asp Pro Tyr Val Lys Glu Ala Glu  
 20 25 30

Asn Leu Lys Lys Tyr Phe Asn Ala Gly His Ser Asp Val Ala Asp Asn  
 35 40 45

Gly Thr Leu Phe Leu Gly Ile Leu Lys Asn Trp Lys Glu Glu Ser Asp  
 50 55 60

Arg Lys Ile Met Gln Ser Gln Ile Val Ser Phe Tyr Phe Lys Leu Phe  
 65 70 75 80

Lys Asn Phe Lys Asp Asp Gln Ser Ile Gln Lys Ser Val Glu Thr Ile  
 85 90 95

Lys Glu Asp Met Asn Val Lys Phe Phe Asn Ser Asn Lys Lys Lys Arg  
 100 105 110

Asp Asp Phe Glu Lys Leu Thr Asn Tyr Ser Val Thr Asp Leu Asn Val  
 115 120 125

Gln Arg Lys Ala Ile His Glu Leu Ile Gln Val Met Ala Glu Leu Ser  
 130 135 140

Pro Ala Ala Lys Thr Gly Lys Arg Lys Arg Ser Gln Met Leu Phe Arg  
 145 150 155 160

Gly Arg Arg Ala Ser Gln Gly Gly Gly Gly Ser Gly Gly Gly Gly Ser  
 165 170 175

Gly Gly Gly Gly Ser Met Tyr Arg Met Gln Leu Leu Ser Cys Ile Ala  
 180 185 190

Leu Ser Leu Ala Leu Val Thr Asn Ser Ala Pro Thr Ser Ser Ser Thr  
 195 200 205

Lys Lys Thr Gln Leu Gln Leu Glu His Leu Leu Leu Asp Leu Gln Met  
 210 215 220

Ile Leu Asn Gly Ile Asn Asn Tyr Lys Asn Pro Lys Leu Thr Arg Met  
 225 230 235 240

Leu Thr Phe Lys Phe Tyr Met Pro Lys Lys Ala Thr Glu Leu Lys His  
 245 250 255

Leu Gln Cys Leu Glu Glu Glu Leu Lys Pro Leu Glu Glu Val Leu Asn  
 260 265 270

Leu Ala Gln Ser Lys Asn Phe His Leu Arg Pro Arg Asp Leu Ile Ser  
 275 280 285

Asn Ile Asn Val Ile Val Leu Glu Leu Lys Gly Ser Glu Thr Thr Phe  
 290 295 300

Met Cys Glu Tyr Ala Asp Glu Thr Ala Thr Ile Val Glu Phe Leu Asn  
 305 310 315 320

Arg Trp Ile Thr Phe Cys Gln Ser Ile Ile Ser Thr Leu Thr  
 325 330

<210> 19

<211> 334

<212> PRT

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: fusion murine  
 IFN-g/linker/murine IL-2"

<400> 19

Met Asn Ala Thr His Cys Ile Leu Ala Leu Gln Leu Phe Leu Met Ala  
 1 5 10 15

Val Ser Gly Cys Tyr Cys His Gly Thr Val Ile Glu Ser Leu Glu Ser  
 20 25 30

Leu Asn Asn Tyr Phe Asn Ser Ser Gly Ile Asp Val Glu Glu Lys Ser  
 35 40 45

Leu Phe Leu Asp Ile Trp Arg Asn Trp Gln Lys Asp Gly Asp Met Lys  
 50 55 60

Ile Leu Gln Ser Gln Ile Ile Ser Phe Tyr Leu Arg Leu Phe Glu Val  
 65 70 75 80

Leu Lys Asp Asn Gln Ala Ile Ser Asn Asn Ile Ser Val Ile Glu Ser  
 85 90 95

His Leu Ile Thr Thr Phe Phe Ser Asn Ser Lys Ala Lys Lys Asp Ala  
 100 105 110

Phe Met Ser Ile Ala Lys Phe Glu Val Asn Asn Pro Gln Val Gln Arg  
 115 120 125

Gln Ala Phe Asn Glu Leu Ile Arg Val Val His Gln Leu Leu Pro Glu  
 130 135 140

Ser Ser Leu Arg Lys Arg Lys Arg Ser Arg Cys Gly Gly Gly Gly Ser  
 145 150 155 160

Gly Gly Gly Gly Ser Met Tyr Ser Met Gln Leu Ala Ser Cys Val Thr  
 165 170 175

Leu Thr Leu Val Leu Leu Val Asn Ser Ala Pro Thr Ser Ser Ser Thr  
 180 185 190

Ser Ser Ser Thr Ala Glu Ala Gln Gln Gln Gln Gln Gln Gln Gln  
 195 200 205

Gln Gln Gln His Leu Glu Gln Leu Leu Met Asp Leu Gln Glu Leu Leu  
 210 215 220

Ser Arg Met Glu Asn Tyr Arg Asn Leu Lys Leu Pro Arg Met Leu Thr  
 225 230 235 240

Phe Lys Phe Tyr Leu Pro Lys Gln Ala Thr Glu Leu Lys Asp Leu Gln  
 245 250 255

Cys Leu Glu Asp Glu Leu Gly Pro Leu Arg His Val Leu Asp Leu Thr  
 260 265 270

Gln Ser Lys Ser Phe Gln Leu Glu Asp Ala Glu Asn Phe Ile Ser Asn  
 275 280 285

Ile Arg Val Thr Val Val Lys Leu Lys Gly Ser Asp Asn Thr Phe Glu  
 290 295 300

Cys Gln Phe Asp Asp Glu Ser Ala Thr Val Val Asp Phe Leu Arg Arg  
 305 310 315 320

Trp Ile Ala Phe Cys Gln Ser Ile Ile Ser Thr Ser Pro Gln  
 325 330

<210> 20

<211> 26

<212> DNA



<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: sense primer for cloning murine IL-2"

<400> 20

cggaattcca cagtgcctc aagtc

26

<210> 21

<211> 24

<212> DNA

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: antisense primer for cloning murine IL-2"

<400> 21

ggggtacccc ttatgtgttg taag

24

<210> 22

<211> 34

<212> DNA

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: sense primer for cloning variant N88G of murine IL-2"

<400> 22

gagaatttca tcagcgtat cagagtaact gttg

34

<210> 23

<211> 34

<212> DNA

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: antisense primer for cloning variant N88G of murine IL-2"

<400> 23  
caacagttac tctgataccg ctgatgaaat tctc

34

<210> 24

<211> 34

<212> DNA

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: sense primer for cloning variant N88R of murine IL-2"

<400> 24  
gagaatttca tcagccgtat cagagtaact gttg

34

<210> 25

<211> 34

<212> DNA

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: antisense primer for cloning variant N88R of murine IL-2"

<400> 25  
caacagttac tctgatacgg ctgatgaaat tctc

34

<210> 26

<211> 43

<212> DNA

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: sense primer for cloning variant Q126M of murine IL-2"

<400> 26  
ggagatggat agccttctgt atgagcatca tctcaacaag ccc 43

<210> 27

<211> 43

<212> DNA

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: antisense primer  
for cloning variant Q126M of murine IL-2"

<400> 27  
gggcttggtg agatgatgct catacagaag gctatccatc tcc 43

<210> 28

<211> 27

<212> DNA

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: sense primer for  
cloning variant D20I of murine IL-2"

<400> 28  
gagcagctgt tgatgacct acaggag 27

<210> 29

<211> 27

<212> DNA

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: antisense primer  
for cloning variant D20I of murine IL-2"

<400> 29  
ctcctgtagg atcatcaaca gctgctc 27

<210> 30

<211> 35

<212> DNA

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: sense primer for cloning murine IL-7"

<400> 30

ccgctcgagc ggatgttcca tgtttctttt agata

35

<210> 31

<211> 33

<212> DNA

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: antisense primer for cloning murine IL-7"

<400> 31

cggggtaccc cggtatatac tgcccttcaa aat

33

<210> 32

<211> 32

<212> DNA

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: sense primer for cloning murine IL-18"

<400> 32

ccgctcgagc ggatggctgc catgtcagaa ga

32

<210> 33

<211> 43

<212> DNA

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: antisense primer for cloning murine IL-18"

<400> 33

cggggtaccc cgctaacttt gatgtaagtt agtgagagtg aac

43

<210> 34

<211> 43

<212> DNA

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: sense primer for cloning variant K89A of murine IL-18"

<400> 34

ccagactgat aatatacatg tacgcagaca gtgaagtaag agg

43

<210> 35

<211> 43

<212> DNA

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: antisense primer for cloning variant K89A of murine IL-18"

<400> 35

cctcttactt cactgtctgc gtacatgtat attatcagtc tgg

43

<210> 36

<211> 50

<212> DNA

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: sense primer for cloning mature murine IL-18"

<400> 36  
ggtaggagcg gttaggcgg aggtggctct aactttggcc gacttcactg 50

<210> 37

<211> 31

<212> DNA

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: antisense primer for cloning mature murine IL-18"

<400> 37  
ctaactttga tgtaagttag tgagagtga c 31

<210> 38

<211> 32

<212> DNA

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: sense primer for cloning murine IL-21"

<400> 38  
ccgctcgagc ggatggagag gacccttgctc tg 32

<210> 39

<211> 37

<212> DNA

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: antisense primer for cloning murine IL-21"

<400> 39  
cggggtaccc cgctaggaga gatgctgatg aatcatc 37

<210> 40

<211> 32

<212> DNA

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: sense primer for cloning murine IL-15"

<400> 40  
ccgctcgagc ggatgtacag catgcagctc gc 32

<210> 41

<211> 31

<212> DNA

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: antisense primer for cloning murine IL-15"

<400> 41  
cggggtaccc cgctacttgt catcgctgctc c 31

<210> 42

<211> 32

<212> DNA

<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: primer 5' for generating the mIL2/IL18 fusion"

<400> 42  
ccgctcgagc ggatgtacag catgcagctc ga 32

<210> 43  
 <211> 50  
 <212> DNA  
 <213> artificial sequence  
 <220>  
 <221> source  
 <223> /note= "Description of artificial sequence: 5' linker primer  
 for generating the lIL2/IL18 fusion"

<400> 43  
 ggtggaggcg gttcaggcgg aggtggctct atggctgccca tgtcagaaga 50

<210> 44  
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 for generating the mIL2/IL18 fusion"

<400> 44  
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 for generating the mIL18/IL2 fusion"

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<213> artificial sequence

<220>

<221> source

<223> /note= "Description of artificial sequence: 3' linker primer for generating the mIL18/IL2 fusion"

<400> 46

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<211> 31

<212> DNA

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<220>

<221> source

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<210> 48

<211> 50

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<220>

<221> source

<223> /note= "Description of artificial sequence: sequence for generating the mIL2/mature IL18 fusion"

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<210> 49

<211> 31

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<220>

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<223> /note= "Description of artificial sequence: 5' linker primer  
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<210> 51

<211> 49

<212> DNA

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<220>

<221> source

<223> /note= "Description of artificial sequence: 3' linker primer  
for generating the mIL7/IL2 fusion"

<400> 51  
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<210> 52

<211> 50

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<223> /note= "Description of artificial sequence: 5' linker primer  
for generating the mIL2/IL21 fusion",

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<210> 53  
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 for generating the mIL21/IL2 fusion"

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<210> 54  
 <211> 55  
 <212> DNA  
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 for generating the mIL2/IFNg fusion"

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<210> 55  
 <211> 33  
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<400> 55  
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<210> 56  
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<220>

<221> source

<223> /note= "Description of artificial sequence: 5' primer for cloning the mIFNg/IL2 fusion"

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37

<210> 57

<211> 49

<212> DNA

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<220>

<221> source

<223> /note= "Description of artificial sequence: 3' linker primer for generating the mIFNg/IL2 fusion"

<400> 57

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49

<210> 58

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50

<210> 59

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<223> /note= "Description of artificial sequence: 3' linker primer  
for generating the mIL15/IL2 fusion"

<400> 59

agagccacct ccgcctgaac cgcctccacc cttgtcatcg tcgtccttg

49